DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 10/06/09. Claims 1-12 are currently pending in the application. Accordingly, claims 1-12 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Applicant's argument with respect to the rejection of claims 1 and 3-12 under 35 U.S.C. 112, first paragraph has been fully considered. While applicant provided support and demonstrated enablement for m=3, 5, and 7, the Examiner maintains that applicant does not have support for m=4 or m=6. As a result, the Examiner maintains that applicant does not have written support for such range. Consequently, the rejection of claims 1 and 3-12 under 35 U.S.C. 112, first paragraph is therefore maintained.

Applicant's contention that the Examiner is oversimplifying the M.P.E.P. recitation that an extension by one carbon is expected to result in compounds with similar properties has been fully considered but is not found persuasive. Applicant further argues that the properties at issue are biological activities. Such arguments are however without merit as independent claim 1 is directed to a water-soluble fullerene polycarboxylic acid of a pharmaceutically acceptable cation with a particular formula.

Gan et al. teach fullerene derivative that are water-soluble (just like applicant's) and that are air-stable. Gan et al. do not teach that m=3 or that the aforementioned compounds are to be formulated as pharmaceutical agents. The Examiner however contends that according to M.P.E.P. 2144.09, a *prima facie* case of obviousness can indeed be made when chemical compounds have very close structural similarities. In fact, it is taught that homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). Thus, regardless of the type of properties being purported by applicant, the Examiner maintains that absent of unexpected results demonstrating otherwise, the fullerene derivatives of Gan would necessarily possess similar biological functions as the instant compounds. Because Gan did not explicitly teach that his compounds could be formulated into particular pharmaceutical formulations, Chiang et al. were therefore provided to demonstrate that fullerene derivatives can be prepared as pharmaceutical formulations and that such formulations can further contain excipients and carriers.

While applicant argues that a much more complex interaction is at play in this instant invention as opposed to the simple chemical properties reported in the aforementioned case law, the Examiner maintains that the case law does not recite any distinction between a complex interaction and a simple interaction. Rather, the case law is explicit in its recitation that homologs would necessarily possess the same properties regardless of the type of properties being investigated. If, however, applicant

believes otherwise, it is incumbent upon applicant to demonstrate via comparative results that the derivatives of Gan are in fact not biologically active and in fact cannot be made into pharmaceutical compositions. As for applicant's arguments that Gan's sole utility is that such compounds are to be used as precursors for further derivatizaion, such arguments are not persuasive as Gan teaches various utilities for fullerene derivatives and further teach that his fullerene derivatives may be (i.e. not required) used as precursors for further derivatization studies (see pg. 275, paragraph 1 and pg. 277, last paragraph). In fact, given that Gan et al. explicitly teach that few water-soluble fullerene derivatives are known, the Examiner contends that the desire to formulate pharmaceutical compositions would have prompted one of ordinary skill in the art to utilize the fullerenes of Gan in pharmaceutical formulations since they are water-soluble.

As for applicant's arguments that the mere fact that some fullerenes are scavenging free radicals would not motivate one of ordinary skill in the art to formulate any other fullerene derivatives into pharmaceutical compositions, such arguments are not persuasive as the Examiner again reiterates the fact that Chiang was provided to demonstrate that fullerene derivatives, derivatives similar to Gan, can be made into pharmaceutical compositions. Moreover, the Examiner refers applicant to Gan et al. who teach the various utilities for fullerene derivatives thus prompting one of ordinary skill to formulate such compounds into pharmaceutical compositions if the desire is to obtain useful pharmaceutical formulations of such compounds. Additionally, the Examiner reminds applicant that solubility is an important parameter in pharmaceutical formulations when determining adequate amount of drug that may be available for oral

absorption, permeability, and transit time *in vivo*. As a result, the Examiner maintains that Gan in view of Chang does indeed render obvious applicant's invention.

Applicant's argument with respect to the rejection of claims 2 and 5-6 in further view of Miller has again been fully considered but is not found persuasive. Applicant argues that the relative amounts of fullerene and amino acid that are brought into reaction are not specified by Miller. Such arguments are however not persuasive as Miller et al. teach similar method of preparation of applicant delineated in claim 2. While applicant argues that Miller et al. do not teach any amount, the Examine respectfully points out that Applicant also does not recite any particular amount of fullerene or amino acids to be used in the aforementioned claims. Additionally, because Miller et al. do not teach addition of solubilizer to the method, the Examiner contended that such addition would have been within the purview of the skilled artisan if the desire is to enhance the solubilization of the fullerene derivatives in water.

While applicant argues that the instant invention is directed to a product obtained by poly-addition of 2 to 12 amino acid molecules, the Examiner maintains that such arguments do not commensurate in scope with the claims as the claims do not recite poly-addition of 2 to 12 amino acids. As a result, the Examiner maintains that Miller in view of the Examiner's contention did indeed render obvious applicant's instant claimed invention. Moreover, the Examiner maintains that because Miller demonstrated that fullerene derivatives were effective in inhibiting HIV and CMV, one of ordinary skill in the art would have indeed found it obvious to try the compounds of Gan for inhibition

HIV and CMV with a reasonable expectation of success given that Gan and Miller's compounds are structurally similar and would thus have expected to possess similar properties.

As for applicant's arguments regarding the lack of *in vivo* effect of the compounds of Miller, the Examiner again reiterates the fact that the claims are directed to a method of inhibiting virus reproduction, such recitation does not require that the treatment be in vivo. Even if arguendo the instant claims required *in vivo* treatment, such treatment would be well within the skilled artisan as it would have been obvious to one skilled in the art to treat patients (i.e. in vivo administration) given that Miller et al. demonstrated that the compounds of the invention were effective *in vitro* and thus the next logical step would be to treat HIV and CMV affected patients. As a result, the Examiner contends that the rejection of record was indeed proper and is therefore maintained.

For the foregoing reasons, the rejections of record were indeed proper and are therefore maintained. However, in view of applicant's amendment, the following modified 103 (a) Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated by the court in Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), regarding the written description requirement:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

In this instant application, applicant did not specifically describe a polycarboxylic anion acid salt wherein m is an integer of 4 or 6 (see claim 1, line 8, m ranges from 3 to 7). While applicant provided support and demonstrated enablement for m=3, 5, and 7, the Examiner maintains that applicant does not have support for m=4 or m=6. As a result, the Examiner maintains that applicant has not provided sufficient written support for such range. Consequently, due to this lack of written description, the exact interpretation of "m is an integer from 3 to 7" being claimed by applicant cannot be fully ascertained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-4, and 11-12 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Gan et al. (Chinese Chemical Letters, 1994, Vol. 5, No. 4, pgs. 275-278, previously cited) in view of Chiang et al. (U.S.5,648,523, previously cited).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Gan et al. teach water-soluble fullerene derivatives that are air-stable (see abstract and pg. 277, last paragraph). In particular, Gan et al. teach that ß-alanine sodium salt reacts with C_{60} to give a water-soluble derivative A: $C_{60}(NHCH_2CH_2COO^-Na^+)_x(H)_x$ (i.e. a polycarboxylic anion where m is equal to 2; see pg. 276, top paragraph). Importantly, Gan et al. teach that elemental analysis reveals that x is equal to 9 (i.e. n is 9) and this necessarily reads on the claim limitation where n is an integer from 2 to 12 (see pg. 275, abstract and pg. 276, paragraph 2).

Gan et al. do not teach fullerene derivatives where m is at least 3. Similarly, Gan et al. do not teach the fullerene derivatives in pharmaceutical compositions or formulated as tablets or injections.

The Examiner however contends that it is well within the purview of the skilled artisan to extend the alkyl chain by one carbon as extension by one carbon is expected to result in compounds with similar properties absent of unexpected results (instant claims 1 and 11-12).

Chiang et al. teach fullerene derivatives as free-radical scavengers (see abstract). Importantly, Chiang et al. teach that the fullerene derivatives can be prepared as pharmaceutical formulations which contain an excipient (see col. 5, lines 5-7 and col. 6, lines 26-29). In particular, Chiang et al. teach that the active ingredients can be associated with a carrier which constitutes one or more accessory ingredients (see col.

6, lines 39-43). Chiang et al. further teach that the formulations can be made as tablets or powders wherein the active ingredients are blended with finely divided solid carriers which necessarily include fillers (instant claims 3-4; see col. 6, lines 44-47).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to try the fullerene derivatives of Gan et al. as pharmaceutical compositions and formulate them in the form of tablets and injections given that Chiang et al. teach that formulations of fullerene derivatives as pharmaceutical compositions and in the form of tablets are known in the art. Additionally, one of ordinary skill in the art would have found it obvious to extend the alkyl chain attached to the fullerene compound by 1 carbon chain since one of ordinary skill in the art would have expected that extension of the alkyl chain by 1 carbon would have led to compounds of similar properties. Moreover, one of ordinary skill in the art would have found it obvious to try and formulate the modified compositions of Gan et al. as suppositories or injections since these types of formulations are well-known formulations in the pharmaceutical art. Thus, given the teachings of Gan and Chiang, one of ordinary skill would have been motivated to formulate the derivatives of Gan as pharmaceutical compositions and in the form of tablets with the reasonable expectation of providing fullerene derivatives that are soluble in water and air-stable.

Claims 2 and 5-6 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Gan et al. (Chinese Chemical Letters, 1994, Vol. 5, No. 4, pgs. 275-278,

previously cited) in view of Miller et al. (RU 2196602 C1, cited by applicant and filed on an IDS 1449).

The Gan reference is as discussed above and incorporated by reference herein. However, Gan et al. do not teach the method of inhibiting virus reproductions using the aforementioned fullerene derivatives. Likewise, Gan et al. do not teach a method of preparing fullerene derivatives.

Miller et al. teach compounds prepared by a single-stage synthesis via direct addition of the residues of amino acids or dipeptides to the fullerene core (see pg. 2, lines 1-2). This is done by adding to a solution of fullerene in o-dichlorobenzene aqueous solution of sodium salt or potassium salt of an amino acid especially aminocaproic and aminobutyric, and 18-crown-6 (instant claim 2; see pg. 2, lines 2-5). The reaction mass is stirred for 6-8 hours at 60ºC (instant claim 2; see pg.2, line 5). Particularly, Miller et al. teach that the compounds of the invention possess the ability to inhibit HIV and CMV simultaneously (see pg. 3, lines 3-5 and claims 2-3). Additionally, Miller et al. teach that the compounds are able to block the synthesis of structural protein of CMV thereby suggesting inhibition of viral reproduction (instant claims 5-6; see pg. 3, lines 7-8).

Moreover, the examiner contends that while Miller et al. are silent to the addition of a solubilizer in the method of preparing the fullerene derivatives, it would have been well within the purview of the skilled artisan to add solubilizing agents to the method of

preparing the fullerene derivatives in order to enhance the solubilization of the aforementioned compounds in water.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to prepare the modified compound of Gan et al. as taught by Miller et al. and further add solubilizing agents such as PEG agents to the composition in order to enhance the water solubility of the compounds. Additionally, one of ordinary skill in the art would have found it obvious to try the modified compounds of Gan et al. for inhibiting HIV and CMV since Miller et al. teach that similar compounds possess such properties and in view of the fact that similar compounds are expected to possess similar characteristics and/or properties. Thus, given the teachings of Gan and Miller, one of ordinary skill would have been motivated to try the compounds of Gan in view of Miller for inhibition of HIV and CMV with the reasonable expectation of providing fullerene derivatives that are soluble in water and compounds that inhibit both HIV and CMV simultaneously.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

01/12/2010

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627